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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,782	07/09/2001	Susan Hardin	0007/01UTL	9388

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EXAMINER

SMITH, CAROLYN L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/901,782

Applicant(s)

HARDIN ET AL.

Examiner

Carolyn L Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2003 and 11 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 25-34 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6, 10-17 and 43 is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-9, 18-24, 35-42 and 45-46 is/are rejected.
- 7) ☒ Claim(s) 7 and 44 is/are objected to.
- 8) ☒ Claim(s) 1-46 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 07072003.
- 4) ☒ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. 10072003.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's amendments and remarks, filed 12/5/03 and 3/11/04, are acknowledged. Amended claims 1-2, 6-7, 10-12, 16-18, 20-21, and 24 and new claims 35-46 are acknowledged.

Applicant's arguments, filed 12/5/03 and 3/11/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The interview summary provided by Applicants, filed 12/5/03, is accepted by the Examiner.

The information disclosure statement filed 7/7/03 (originally filed 4/17/03) fails to comply with the provisions of 37 CFR 1.97, 1.98, and MPEP § 609, because the PCT International Search Report is not a published document. It has been looked at by the Examiner but is not formally acknowledged as being considered on the merits.

Claims 1-24 and 35-46 are herein under examination.

### ***Claim Objections***

Claim 7 is objected to because of the following informality: There is a misplaced "d" on line 3 of claim 7. Appropriate correction is required. This objection is necessitated by amendment.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-24 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by amendment.

Claim 20 recites the phrase "two different sites" which does not appear to have support in the specification. Due to the introduction of this phrase without appropriate support in the specification, claims, or drawings as originally filed, this phrase is considered to be NEW MATTER. Claims 21-24 and 45 are also rejected due to their direct or indirect dependency from claim 20. This rejection is necessitated by amendment.

***Claims Rejected Under 35 U.S.C. § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 19 is maintained and newly applied to new claims 18, 35-42, and 46 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 19 (line 3) and new claim 42 (line 3) recite the phrase "mixtures or combinations thereof of the *Taq* polymerase" which is vague and indefinite. It is unclear what else may be included in these multiple entities besides *Taq* DNA polymerase I. Clarification of the metes and bounds of these claims via clearer claim wording is required. Applicants state this unclear phrase has been removed from claim 19, but it has not been removed. This rejection is maintained (claim 19) and necessitated by amendment (claim 42).

Claims 18, 35, and 36 are vague and indefinite due to the unclarity of citing an abbreviation, such as FRET. Correction is suggested by amending in of the full name in parentheses. Claims 37-42 and 46 are also rejected due to its dependency from claims 35 and 36. This rejection is necessitated by amendment.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-5, 7-9, and 20-23 is necessitated by amendment under 35 U.S.C. 102(a) and (b) as being anticipated by Williams (WO 00/36151 under 102(a)) and Brandis (Nucleic Acids Research, 1999, Vol. 27, No. 8 under 102(b)).

This rejection is necessitated by amendment and reiterated for reasons of record. This rejection is made with the assumption that the phrase “two different sites” recited in instant claim 20 will be removed due to the presence of NEW MATTER.

Applicants state the tag on the polymerizing agent is not a substrate transiently held within the active site of the polymerizing agent during monomer incorporation, but is an atomic or molecular species that is part of the polymerizing agent. This is found unpersuasive as the claims fail to state that such a transient nature is excluded from the limitations. Therefore, the claims will be interpreted broadly and reasonably to include a transient nature of the composition. Applicants state there is no suggestion to covalent bonding a tag to the polymerizing agent itself. This is found unpersuasive as covalent bonding is discussed in the rejection below, and Applicants fail to present evidence that would render the rejection improper. Applicants state the present invention generates natural sequences instead of modified sequences. This is found unpersuasive as this potential aspect of their invention is not stated in the instant

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claims. Applicants make another assertion that the Williams/Brandis prior art do not disclose a polymerase having a covalently bound fluorescent tag that is directly involved in monitoring dNTP incorporation. This is found unpersuasive as the instant claims also fail to state that the tag is directly involved in monitoring dNTP incorporation. Claims 1-5, 7-9, and 20-23 as broadly and reasonably interpreted are anticipated by the Williams/Brandis prior art, as discussed below.

As stated in the previous Office action, mailed 9/10/03, Applicants stated the critical difference between their invention and the prior art is that the tags in their invention remain associated with the polymerizing agent. This was found unpersuasive as the claims, as written, state a polymerizing agent and a tag without mention of whether this tag is transient or permanent. Applicants stated the Williams/Brandis prior art references did not disclose a tagged polymerizing agent. This is found unpersuasive as bonding inherently occurs between the polymerase and the tagged entity, as described, *infra*. Even though this bonding may occur transiently, it does occur which is encompassed in the broad reasonable interpretation of the tagged polymerase agent.

Williams discloses a *Taq* DNA polymerase (p. 8, lines 23-28) in which a fluorescently labeled dNTP (tag) is associated with the polymerase during monomer incorporation (p. 8, lines 1-9). Williams discloses a fluorophore and quencher pair being incorporated into oligo probes (p. 2, lines 16-18). The dNTP tag consists of a labeled nucleotide triphosphate (NTP) having a  $\gamma$ -phosphate with a fluorophore moiety attached and a quencher moiety that sufficiently prevents fluorescence until incorporation of the NTP at which time the  $\gamma$ -phosphate with the fluorophore moiety is released and detected (p. 8, lines 10-20). As Webster's II New Riverside Dictionary

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defines a tag as a piece of something that identifies, classifies or labels; one reasonable interpretation of the quencher is a tag whose close presence to the fluorophore tag results in fluorescent signal disappearance (p. 2, lines 16-25). Williams discloses the fluorescence is detected when labeled dNTPs are incorporated into the strand and fluorescence is induced (p. 9, lines 28-29). Williams discloses that upon incorporation, the fluorescent dye molecule is released with pyrophosphate from the polymerase and then swept away from the parent DNA molecule by the flow (p. 10, lines 13-17), suggesting the polymerase's detectable property reverts back to its initial state. Williams discloses that as the polymerase moves along the DNA, the nucleotide sequence is read from the order of released dyes (p. 14, lines 30-31). Williams discloses the possible presence of other polymerases, such as HIV reverse transcriptase, as stated in claims 5, 9, and 23. Williams discloses acquiring a sequence of images/movies (read outs) of fluorophores in order to track the path of single dyes involved in monomer incorporation (page 8, first paragraph; page 12, third paragraph; page 13, second paragraph; page 14, fourth paragraph) as well as data storage units that record detection (page 15, second and third paragraphs).

A 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to show that a characteristic not disclosed in the reference is inherent (see MPEP 2131.01 (c)). Brandis discloses a *Taq* DNA polymerase I including an inherent characteristic that polymerases go through conformational changes (abstract). Brandis also discloses that a change occurs in a fluorescent label during the change in conformational states of the polymerase when nucleotide binding occurs as the polymerase is active (abstract). Voet et al. disclose a transition state theory allowing the understanding of how enzymes catalyze



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reactions (p. 332, col. 2, first paragraph). Voet et al. disclose a high-energy (unstable) complex existing with covalent bonds during a bimolecular reaction (p. 332, col. 2, second paragraph).

Thus, Williams and Brandis anticipate claims 1-5, 7-9, and 20-23 of the instant invention.

### ***Conclusion***

Claims 6, 10-17, and 43 are allowable.

Claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

May 13, 2004

*Ardin H. Marschel* 6/6/04  
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REGISTERED MAILER